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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,912	03/05/2002	Richard R. Bott	GC724	9189

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/091,912	BOTT ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *4-8,11,16-18 and 20-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,9,10,12-15,19 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *08/29/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Application

[1] Claims 1-29 are pending in the application.

[2] Applicants' amendment to the claims filed December 19, 2003 is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

Election/Restriction

[3] Applicants' election with traverse of the invention of Group VI, claims 1-3, 9-10, 12-15, 19, and 27-29, drawn to a cutinase variant having a substitution of Ile at position 178, Phe at position 180, and Ser at position 205 of SEQ ID NO:2, filed December 19, 2003, is acknowledged. Applicants traverse the restriction requirement by arguing that "the same basic search will be done for all of the Claims (*i.e.,* SEQ ID NO:2), and the Claims are all in the same class and subclass, Applicants respectfully submit that there should be no added burden on the Examiner to search multiple Groups at the same time" (see page 6 of the response). Applicants' argument is not found persuasive.

Contrary to applicants' assertion, each of the inventions listed as Groups I-XII requires a *separate search*. If a search for each of Groups I-XII required only a search for SEQ ID NO:2, then a separate search would not be required. However, each of the individual inventions of Groups I-XII is structurally distinct from the others based on their unique amino acid variations and each of the inventions requires a separate and independent patent and non-patent literature and sequence search. Therefore, a

serious burden would be required to co-extensively search and examine all of the inventions listed as Groups I-XII.

[4] The requirement is still deemed proper and is therefore made FINAL.

[5] It is noted that applicants state, "[t]he Examiner further requires a species election" at page 5 of the response. However, the instant restriction requirement is NOT an election of species and nowhere does the Office action mailed November 18, 2003 indicate that the requirement is an election of species.

[6] It is further noted that the claims were restricted based on the original claim set filed March 05, 2002. There is a discrepancy in the claims filed March 05, 2002 and the amended claims filed December 19, 2003 as follows: claim 12 of the claims filed December 19, 2003 does not correspond with claim 12 of the original claims filed March 05, 2002. Instead, claim 12 of the amended claims filed December 05, 2002 corresponds to claim 13 of the claims filed March 05, 2002. Because of this, claim 16 of the claims filed March 05, 2002, no longer belongs in the elected group and belongs with Group I instead.

[7] Claims 4-8, 11, 16-18, and 20-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

[8] Claims 1-3, 9-10, 12-15, 19, and 27-29 are being examined to the extent the claims read on the elected invention.

Information Disclosure Statement

[9] All references cited by applicants in the information disclosure statement (IDS) filed August 29, 2003 have been considered by the examiner. A copy of the IDS is attached to the instant Office action.

Specification/Informalities

[10] The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "Mutant *Pseudomonas mendocina* Cutinase Polypeptide".

[11] The specification is objected to as the specification describes Table 1 as being color coded (see pages 13-14 of the specification). However, Table 1 is in black and white, *i.e.,* there are no color codes as asserted in the specification.

[12] The use of the trademarks "Quik-Change™" and "Excel™" have been noted in this application (see pages 7, 10 and 13 of the specification). They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

[13] Claims 10 and 14 are objected to in the recitation of "Glyc" (claim 10) and "Phy 180" (claim 14). It appears the terms should be replaced with "Gly" and "Phe", respectively. Appropriate correction is required.

[14] It is noted that claim 13 uses the three letter abbreviation for lysine, *i.e.,* Lys, and uses no abbreviation for leucine. The claim is objected to as the use of an amino acid abbreviation for lysine and no abbreviation for leucine may be a potential source of confusion. In order to avoid any confusion and to maintain the consistent use of three-letter abbreviations for amino acids in the claims, it is suggested that applicant replace "Leucine" with "Leu".

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[15] Claim(s) 2-3, 9-10, 12-15, 19, and 27-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claims 2 and 29 are indefinite in the recitation of "derived from". The meaning of the term is unclear and it is unclear as to those polypeptides that are "derived from" *P. mendocina* or *Pseudomonas* species that are to be encompassed within the scope of the claim and those that are excluded. For purposes of examination, the examiner has interpreted the term as meaning "isolated from". It is suggested that applicant clarify the meaning of the claim.

[b] Claim 3 is confusing in that it is unclear as to how the polypeptide of claim 3 (SEQ ID NO:2) can simultaneously be a variant, having a different amino acid sequence (SEQ ID NO:2 having alterations at one or more of positions 178, 180,

and 205) as recited in claim 1. For purposes of examination, the claim has been interpreted as meaning that SEQ ID NO:2 is the parent, *i.e.,* unmutated, amino acid sequence. It is suggested that applicant clarify the meaning of the claim.

[c] Claims 9 and 27 are indefinite in the recitation of "stability". Stability can have a plurality of meanings, *e.g.,* thermostability and/or pH stability. As such, it is unclear as to applicants' intended meaning of the term and consequently, the scope of claimed cutinase variants. It is suggested that applicants clarify the meaning of the term.

[d] The terms "enhanced stability" in claims 9 and 27, "enhanced polyesterase activity" in claims 12-15 and 19, and "thermostable" in claim 28 are unclear absent a statement defining to what the stability, polyesterase activity, or thermostability is being compared. The terms are relative terms and the claims should define and clearly state as to what the stability, polyesterase activity, or thermostability is being compared, *e.g.,* enhanced stability as compared to the *Pseudomonas mendocina* cutinase of SEQ ID NO:2.

[e] Claim 10 is indefinite in the recitation of "Phe is substituted" and "Ser is substituted" as it is unclear as to which Phe and Ser of SEQ ID NO:2 is substituted. A visual inspection of SEQ ID NO:2 indicates that there are at least 8 different Phe residues and at least 23 different Ser residues in SEQ ID NO:2 and it is unclear from the claim as to which of these are meant to be mutated and which of these are not.

[f] Claim 10 recites the limitation "the Ser". There is insufficient antecedent basis for this limitation in the claim. It is suggested that applicants provide antecedent basis for the limitation.

[g] Claims 13-15, 19, and 27 are confusing in that the claims identify residues of SEQ ID NO:2 that are to be mutated, *i.e.,* Ile178, Phe180, and Ser205. However, a visual inspection of the amino acid sequence disclosed in SEQ ID NO:2 and Figure 18 indicates that the recited amino acid positions do not correspond with the amino acids of SEQ ID NO:2 and Figure 18 (see figure below excerpted from SEQ ID NO:2).

```
Arg Gln Gln Gly Pro Met Phe Leu Met Ser Gly Gly Gly Asp Thr Ile
            180                 185                 190
Ala Phe Pro Tyr Leu Asn Ala Gln Pro Val Tyr Arg Arg Ala Asn Val
        195                 200                 205
```

Instead, glutamine is at position 178, glycine is at position 180, and arginine is at position 205 of SEQ ID NO:2 and Figure 18. It appears that SEQ ID NO:2 has an additional 14 amino acids at the N-terminus relative to the wild-type *P. mendocina* cutinase amino acid sequence and that these 14 additional amino acids were not considered when numbering the mutated amino acids. In order to advance prosecution, the examiner has interpreted the claims as though Ile192 of SEQ ID NO:2 corresponds to Ile178 in the claims, Phe194 of SEQ ID NO:2 corresponds to Phe180 in the claims, and Ser219 of SEQ ID NO:2 corresponds to Ser205 in the claims.

[h] Claim 27 is confusing in the recitation of "substitution of Phe 180 with one of Ile, Leu, Asn, and Pro". This is an improper alternative expression and should

be replaced with, for example, "substitution of Phe 180 with one of Ile, Leu, Asn, or Pro." See MPEP 2173.05(h).

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[16] Claims 1-3, 9-10, 12-15, 19, and 27-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention.

The claims are drawn to a genus of cutinase variants comprising substituting one or more amino acids corresponding to sites 178, 180, and 205 of SEQ ID NO:2 and homologous cutinases thereof, wherein said variant has polyesterase activity. For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a *representative number of species* by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying

characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only the following representative species of cutinase variants: SEQ ID NO:2 with amino acid substitution at positions consisting of 178, 180, and 205. The specification fails to describe any additional representative species of the claimed genus. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". In the instant case, the claimed genus of cutinase variants encompasses species that are widely variant in structure, including (but not necessarily limited to) variants of any cutinase and additional variation at residues of SEQ ID NO:2 besides positions 178, 180, and 205. As such, the disclosure of the representative species of SEQ ID NO:2 with amino acid substitution at positions consisting of 178, 180, and 205 is insufficient to be representative of the attributes and features of *all* species encompassed by the claimed genus of claimed cutinase variants. Given the lack of description of a representative number of cutinase variants, the specification fails to sufficiently describe the claimed invention in such full, clear,

concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[17] Claim(s) 1-3, 9-10, 12-15, 19, and 27-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:2 with amino acid substitution at residues consisting of positions 178, 180, and 205, does not reasonably provide enablement for all variants of SEQ ID NO:2 besides those having substitution at positions 178, 180, and 205 and any homologous variants thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

- The claims are overly broad in scope: The claims are so broad as to encompass *all* variants of SEQ ID NO:2 and any homologous variants thereof. The broad scope of claimed cutinase variants is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims. In this case the disclosure is limited to SEQ ID NO:2 with amino acid substitution at residues consisting of positions 178, 180, and 205.

- The lack of guidance and working examples: The specification provides only a single working example of the claimed polypeptide, i.e., SEQ ID NO:2 with amino acid substitution at residues consisting of positions 178, 180, and 205. This working example fails to provide the necessary guidance for making and the entire scope of claimed/recited polypeptides. The specification fails to provide guidance regarding those amino acids of SEQ ID NO:2 and homolgous sequences thereof that may be altered by substitution, addition, insertion, and/or deletion with an expectation of maintaining the desired activity.

- The high degree of unpredictability in the art: The amino acid sequence of a polypeptide determines the protein's structural and functional properties. Predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within a protein's sequence where modifications can be made with a reasonable expectation of success in obtaining

an encoded polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. In this case, the necessary guidance has not been provided in the specification as explained in detail above. Thus, a skilled artisan would recognize the high degree of unpredictability in making the entire scope of polypeptides having the desired activity.

- The state of the prior art supports the high degree of unpredictability: The state of the art provides evidence for the high degree of unpredictability in altering a polynucleotide sequence with an expectation that the encoded polypeptide will maintain the desired activity/utility. For example, Branden et al. ("Introduction to Protein Structure", Garland Publishing Inc., New York, 1991) teach "[p]rotein engineers frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" (page 247). While it is acknowledged that this reference was published in 1991, to date there remains no certain method for reasonably predicting the effects of even a *single* amino acid mutation on a protein. Such mutations may even completely alter a protein's activity. As a representative example, Witkowski et al. (*Biochemistry* 38:11643-11650) teaches that a single amino acid substitution results in conversion of the parent polypeptide's enzymatic activity from

a beta-ketoacyl synthase to a malonyl decarboxylase (see e.g., Table 1, page 11647). Thus, the prior art acknowledges the unpredictability of altering a protein sequence with an expectation of obtaining a protein having a desired function and discloses that even a single substitution in a polypeptide's amino acid sequence may completely alter the function of a polypeptide.

- The amount of experimentation required is undue: While methods of generating variants of a given polypeptide, *e.g.*, by site-directed mutagenesis, and methods of isolating variants of protein-encoding polynucleotides, *e.g.*,, hybridization, are known, it is not routine in the art to screen for *all* polypeptides having a substantial number of modifications as encompassed by the instant claims. Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[18] As stated above, a visual inspection of the amino acid sequence disclosed in SEQ ID NO:2 and Figure 18 indicates that the recited amino acid positions (Ile178, Phe180, and Ser205) do not correspond with the amino acids of SEQ ID NO:2 and Figure 18. Instead, glutamine is at position 178, glycine is at position 180, and arginine is at position 205 of SEQ ID NO:2 and Figure 18. In order to advance prosecution and for purposes of rejecting the claims under 35 USC §§ 102 and 103, the examiner has interpreted the claims as though Ile192 of SEQ ID NO:2 corresponds to Ile178 in the claims, Phe194 of SEQ ID NO:2 corresponds to Phe180 in the claims, and Ser219 of SEQ ID NO:2 corresponds to Ser205 in the claims.

[19] Claim(s) 1-3, 9, 12, and 28-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Poulouse et al. (US Patent 5,352,594) as evidenced by Boston et al. (*Methods Enzymol* 284:298-317). The claims (in relevant part) are drawn to variants of *Pseudomonas mendocina* cutinase having mutation at Ser205 (actually Ser219) of SEQ ID NO:2. Poulouse et al. teach variants of a *P. mendocina* lipase (columns 3-5) having substitution of Ser205 with various amino acids (see columns 11-14). It is noted that the enzyme of Poulouse et al. appears to have a sequence that is identical to amino acids

15-272 of SEQ ID NO:2, which is described as having lipase activity (column 4, lines 58-62). Boston et al. teach that *P. mendocina* lipase was originally classified as a cutinase (page 298, bottom). This anticipates claims 1-3, 9, 12, and 28-29 as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[20] Claim(s) 10, 13-15, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Poulouse et al. The claims (in relevant part) are drawn to variants of *P. mendocina* cutinase having mutation at positions Phe180 and Ser205 (actually Phe194 and Ser219, respectively) of SEQ ID NO:2.

Poulouse et al. disclose the teachings as described above. Poulouse et al. further teach that the catalytic triad of *P. mendocina* lipase is Ser126, His206, and Asp176 (column 5, middle) and that replacement of amino acid within about 15 angstroms or 6 amino acids N- or C-terminal to a catalytic amino acid will lead to an increase or decrease in the perhydrolysis/hydrolysis ratio and the kinetic constants of the enzyme (column 5, lines 41-57). Poulouse et al. teach that in order to obtain an enzyme with the best ratio or substrate specificity in a desired direction, more than one amino acid substitution can be made (column 6, lines 41-45) and provide an example as follows: a Gly205-Thr207 double mutant had an improved specific activity over a Gly205

mutant (columns 15-16). Poulouse et al. provide methods for generating mutations in the sequence of *P. mendocina* lipase, including double mutants (columns 7-8) and methods for screening mutants for desired properties/activities (columns 8-9).

Therefore, it would have been obvious to one of ordinary skill in the art to mutate position 180 of *P. mendocina* lipase or to further mutate position 180 of the *P. mendocina* lipase position 205 mutants of Poulouse et al. with any amino acid. One would have been motivated to mutate position 180 of *P. mendocina* lipase and to further mutate position 180 of the *P. mendocina* lipase position 205 mutants of Poulouse et al. in order to mutate an amino acid within 6 amino acids of a catalytic amino acid (Asp176 of *P. mendocina* lipase) to obtain a polypeptide having the improved characteristics as described by Poulouse et al. One would have a reasonable expectation of success for mutating position 180 of *P. mendocina* lipase and to further mutate position 180 of the *P. mendocina* lipase position 205 mutants of Poulouse et al. because of the results of Poulouse et al. Therefore, claims 10, 13-15, and 27, drawn to the mutant *P. mendocina* cutinase as described above would have been obvious to one of ordinary skill in the art.

[21] It is noted that Poulouse et al. do not teach that their *P. mendocina* esterase Ser205 variants have enhanced stability or enhanced polyesterase activity. Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional

characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

Conclusion

[22] Status of the claims:

- Claims 1-29 are pending.
- Claims 4-8, 11, 16-18, and 20-26 are withdrawn from consideration.
- Claims 1-3, 9-10, 12-15, 19, and 27-29 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Patent Examiner
Art Unit 1652

01-20-04
DAVID STEADMAN
PATENT EXAMINER